

## **I. AMENDMENTS TO THE CLAIMS**

Please amend the claims as follows: Cancel claims 20, 21, 22, 23, 24, 25, 26, 27, 28, and 29 without prejudice to Applicants' right to file continuation or divisional applications directed to the subject matter thereof.

1. (Original) A method of producing an activated ester of polyethylene glycol (PEG), comprising the step of activating PEG with N,N'-disuccinimidyl oxalate or 1,1'-bis[6-(trifluoromethyl)benzotriazolyl] oxalate under the appropriate conditions.
2. (Original) The method according to claim 1, comprising the step of activating PEG with N,N'-disuccinimidyl oxalate.
3. (Original) The method according to claim 2, wherein the ratio of N,N'-disuccinimidyl oxalate to PEG is 30 :1 or less.
4. (Original) The method of producing a N,N'-disuccinimidyl ester of polyethylene glycol (PEG) according to claim 2, wherein an organic base is used as a catalyst.
5. (Original) The method of producing a N,N'-disuccinimidyl ester of polyethylene glycol (PEG) according to claim 4, wherein the base catalyst is selected from the group consisting of pyridine and N,N'-4-dimethylaminopyridine.
6. (Currently Amended) A method of producing a PEG-nucleophile conjugate conjugating an activated ester of polyethylene glycol (PEG) and a biologically active nucleophile, comprising the steps:
  - (a) providing the PEG active ester of claim 2;
  - (b) providing the biologically active nucleophile; and
  - (c) reacting the PEG active ester of claim 2 and the biologically active nucleophile under appropriate conditions. to form a PEG-nucleophile conjugate.
7. (Currently Amended) A method of producing a PEG-linker-nucleophile conjugate conjugating a PEG-linker and a biologically active nucleophile, comprising the steps :
  - (a) providing the PEG active ester of claim 2;
  - (b) providing a linker;
  - (c) reacting the PEG active ester of claim 2 with a the linker; and

(d) reacting the resulting PEG-linker with a biologically active nucleophile under appropriate conditions. ~~to form a PEG-linker-nucleophile conjugate.~~

8. (Original) The method according to claim 6 or 7 wherein said biologically active nucleophile is a peptide or a protein.

9. (Currently Amended) The method according to claim 8, wherein said PEG active ester is reacted with said peptide or protein in the molar ratio of between 1 and 30 moles active ester to 1 mol peptide or protein or with said linker in the molar ratio of 1 mole active ester to 1 to 10 moles linker.

10. (Original) The method according to claim 7, wherein the PEG-linker(s) conjugate is activated with N,N'-disuccinimidyl oxalate, and subsequently reacted with a peptide or protein in the molar ratio of between 1 and 30 moles active ester to 1 mol peptide or protein to form PEG-linker(s) peptide or protein conjugate.

11. (Original) The method according to claim 1, comprising the step of activating PEG with 1,1'-bis[6-(trifluoromethyl)benzotriazolyl] oxalate.

12. (Original) The method according to claim 11, wherein the ratio of 1,1'-bis[6-(trifluoromethyl)benzotriazolyl] oxalate to PEG is 30 :1 or less.

13. (Original) The method of producing a 1,1'-bis[6-(trifluoromethyl)benzotriazolyl] ester of polyethylene glycol (PEG) according to claim 11, wherein an organic base is used as a catalyst.

14. (Original) The method of producing a 1,1'-bis[6-(trifluoromethyl)benzotriazolyl] ester of polyethylene glycol (PEG) according to claim 13, wherein said base catalyst is selected from the group consisting of pyridine and N,N'-4-dimethylaminopyridine.

15. (Currently Amended) A method of ~~producing a PEG-nucleophile conjugate conjugating an activated ester of polyethylene glycol (PEG) and a biologically active nucleophile~~, comprising the steps:

(a) providing the PEG active ester of claim 11;

(b) providing the biologically active nucleophile; and

(c) reacting the PEG active ester of claim 11 and the biologically active nucleophile under appropriate conditions. ~~to form a PEG-nucleophile conjugate.~~

16. (Currently Amended) A method of ~~producing a PEG-linker-nucleophile conjugate conjugating a PEG-linker and a biologically active nucleophile~~, comprising the steps :

a) providing the PEG active ester of claim 11;

b) providing a linker;

- c) reacting the PEG active ester of claim 11 with a the linker; and
- d) reacting the resulting PEG-linker with a biologically active nucleophile under appropriate conditions. to form a PEG-linker nucleophile conjugate.

17. (Original) The method according to claim 15 or 16 wherein said biologically active nucleophile is a peptide or a protein.

18. (Currently Amended) The method according to claim 17, wherein said PEG active ester is reacted with said peptide or protein in the molar ratio of between 1 and 30 moles active ester to 1 mol peptide or protein or with said linker in the molar ratio of 1 mole active ester to 1 to 10 moles linker.

19. (Original) The method according to claim 16, wherein the PEG-linker(s) conjugate is activated with 1,1'-bis[6-(trifluoromethyl)benzo-triazolyl] oxalate, and subsequently reacted with a peptide or protein in the molar ratio of between 1 and 30 moles active ester to 1 mol peptide or protein to form PEG-linker(s) peptide or protein conjugate.

20. (Canceled)

21. (Canceled)

22. (Canceled)

23. (Canceled)

24. (Canceled)

25. (Canceled)

26. (Canceled)

27. (Canceled)

28. (Canceled)

29. (Canceled)